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Journal of Affective Disorders 86 (2005) 143–150

JOURNAL OF AFFECTIVE DISORDERS

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Research report

A history of major depressive disorder and the response to stress

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Received 26 April 2004; accepted 6 January 2005

Abstract

Background: The occurrence of Major Depressive Disorder (MDD) has been linked to an increased vulnerability to stress. However, the specific behavioral and affective aspects that may underlie this vulnerability to stress have not been well studied.
Methods: This study examined sensitivity to a stress manipulation in 62 participants, 30 with and 32 without a previous episode of MDD. Comparisons were made between those with a history of depression and those without, randomized to either the high or low stress conditions on self-report measures of affect and behavior measures of performance.
Results: A significant interaction was found between depression history and level of stress on measures of self-report tension and behavioral performance on the experimental task. Specifically, those with a history of MDD in the high stress condition reported significantly more tension than other participants. Additionally, participants in the high stress condition without a history of MDD responded to uncontrollable stress by responding at a significantly higher rate on the task while those individuals with a history of MDD responded to uncontrollable stress by maintaining a relatively low level of responding. No differences in self-report depressed affect were found.
Limitations: The study utilized a laboratory stressor in a sample composed primarily of college students.
Conclusions: A history of MDD appears to be associated with an increased sensitivity to uncontrollable stress. This vulnerability may manifest itself in the subjective state of individuals (i.e., tension) or in their behavioral responses to stress.

Keywords: Major depressive disorder; Depression; Learned helplessness; Stress

Initial animal studies of uncontrollable stress led to the theory of learned helplessness (Seligman, 1975). An updated version of this theory asserted that some individuals are more vulnerable to stressors than others and thus more likely to experience depression (Abramson et al., 1978). Animal research using a learned helplessness paradigm continues to be widely used to study genetic factors and environmental factors related to depression (for review, see Norman and McGrath, 2000).

Studies on humans have found increases in self-reported negative affect following exposure to an uncontrollable stressor (e.g., Griffith, 1977). However,

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doi:10.1016/j.jad.2005.01.010

learned helplessness in humans has not been the focus of recent laboratory research and, to date, no studies have investigated the relationship between the experimental manipulation of an uncontrollable stressor and an episode of Major Depressive Disorder (MDD).

In the clinical literature, stressful life events have been found to precede the onset of an episode of MDD (e.g., Surtees et al., 1986). Kendler et al. (1999) reported that some individuals were particularly sensitive to the impact of stressful life events, and these individuals were more likely to (1) self-select more stressful environments and (2) suffer from an episode of MDD following stressful life events than others without a history of MDD. In a study of adolescents, Lewinsohn et al. (1999) found stressful life events predicted first onset of MDD, and the amount of stress preceding the first episode of MDD was significantly greater than the magnitude of stressors associated with a recurrence of MDD. In fact, failure to effectively cope with stress may be a determining factor in who experiences an episode of depression (Akiskal and McKinney, 1973; Caspi et al., 2003). Taken together, these findings imply that a past episode of depression is as an indicator of a heightened sensitivity to stress.

Our first objective was to experimentally manipulate stress and examine whether individuals with a history of MDD respond differently to uncontrollable stressors than those without a history of MDD. It was hypothesized that those with a history of MDD would report more tension and negative affect than those who never experienced an episode of MDD. Furthermore, based on the learned helplessness literature, it was expected that those with a past episode of MDD would display a differential behavioral response when faced with a stressful task.

1. Methods

Men and women were recruited with fliers posted in the University of Colorado campus area. They were recruited as part of a larger research project on psychosocial factors related to mood disorders and alcohol use. Participants are described in Table 1.

All participants were required to meet the following criteria: not currently suffering from MDD or an anxiety disorder (as determined by the Structured Clinical Interview for DiagnosisDSM-IV [SCID], First et al., 1995), never have had bipolar disorder or any psychotic disorders (as determined by self-report of known psychiatric diagnoses and the SCID), and report no hearing loss or medical conditions that would require the avoidance of stressful situations. Based on criteria of other concurrent research projects related to alcohol use, participants were: between 21 and 35 years of age, and drank alcohol at least twice weekly. Finally, one half of the participants needed to meet full criteria for an episode of MDD that was in full remission for at least 2 months prior to the first experimental session.

A total of 77 participants participated in an initial screening session. Thirteen volunteers were excluded because they: met criteria for an anxiety disorder (n=3), met the criteria for bipolar disorder or a psychotic disorder (n=3), met criteria for current MDD (n=3), or did not attend all sessions due to scheduling conflicts (n=6). The remaining 62 participants met all of the criteria. Each was compensated $35.00 for participation.

Efforts were made to obtain equal numbers of men and women with and without a history of depression. Within the past depression condition (no or yes) and gender (male or female), participants were randomly assigned to one of two possible levels of stress (low or high).

1.1. Procedure

Participants attended a 1-h screening session and a 3-h experimental session for a total of approximately 4 h. The experimental session included a practice trial (identical for all participants) and four experimental trials that were either all low or all high stress (depending random assignment).

1.1.1. Practice trial

A 5-min practice trial served two primary purposes: (1) to introduce participants to the basic format of the computerized task; and (2) to assess baseline of task performance prior to the experimental manipulation.

During the practice trial, participants were seated in front of a 12-in. monitor displaying a blank screen with a red background while the experimenter read the instructions for the task informing participants that they were to guess numbers in order to change the color of

Table 1
Descriptive data on sample members for overall sample and each condition

	Low stress without past MDD (n=16)	Low stress with past MDD (n=14)	High stress without past MDD (n=16)	High stress with past MDD (n=16)	Overall (N=62)
Age					
Mean (S.D.)	22.47 (2.45)	23.00 (3.37)	22.50 (2.45)	23.31 (3.59)	22.89 (2.99)
Gender					
Males	9	8	8	8	33
Females	7	6	8	8	29
Ethnicity					
Caucasian	14 (88%)	9 (64%)	16 (100%)	14 (88%)	53 (85%)
Black	0	0	0	0	0
Asian	0	0	0	0	0
Latino	1 (6%)	0	0	1 (6%)	2 (3%)
Native	0	1 (7%)	0	0	1 (2%)
Mixed	1 (6%)	4 (29%)	0	1 (6%)	6 (10%)
Marital status					
Single	14 (88%)	13 (93%)	16 (100%)	13 (81%)	56 (90%)
Married	1 (6%)	0	0	1 (6%)	2 (3%)
Engaged	0	0	0	1 (6%)	1 (2%)
Cohabitating	1 (6%)	1 (7%)	0	1 (6%)	3 (5%)
Employment					
Unemployed	4 (27%)	3 (21%)	0	2 (13%)	9 (15%)
Employed part-time	9 (60%)	8 (57%)	15 (94%)	11 (69%)	43 (70%)
Employed full-time	2 (13%)	3 (21%)	1 (6%)	3 (19%)	9 (15%)
Years of education					
Mean (S.D.)	15.93 (1.67)	16.21 (1.67)	15.13 (3.76)	16.50 (1.32)	15.93 (2.34)
Mean (S.D.)	4.69 (4.03)	9.14 (6.12)	5.78 (4.38)	7.19 (4.86)	6.62 (5.02)
BDI					
Mean (S.D.)	4.69 (4.03)	9.14 (6.12)	5.78 (4.38)	7.19 (4.86)	6.62 (5.02)

the screen. The task was sufficiently difficult to require full attention but easy enough to be solvable within several trials. Each session began with a red screen that turned to white after 15 s. During the first 2 s after hitting the start button, the screen was blank and solid red. Then, a field appeared on the screen that allowed participants to enter numbers as indicated in the instructions. While the screen was red, the participants could guess numbers in an attempt to switch the screen back to white as quickly as possible. The number that comprised the correct response remained the same for five consecutive exposures to the red screen and then changed to a new number. Exposure to the red screen lasted up to 13 s if no correct response was given.

Following a change in screen color from red to white (either by the entry of a correct response or because 13 s had elapsed without a correct response), the computer displayed a blank white screen for a minimum of 15 s. The length of white screen was determined as follows: if no correct response was given while the screen was red, the white screen lasted 15 s; if a correct response was given during the preceding period of exposure to the red screen, the amount of time of exposure to the red screen remaining (i.e., the full 15 s of red screen minus the amount of time of red screen that had elapsed when the correct response was entered) was added on to the standard 15 s for white screen. Thus, the white screen could range from 15 to 28 s. Each cycle of red and white screens lasted 30 s. The number of responses during the red screens was recorded as a behavioral measure of task performance. The screen turned red then white 10 times during the 5-min trial.

1.1.2. Experimental trials

Upon completion of the post-practice trial packet, participants completed four, 10-min trials of the experimental task. Except for the manipulation of stress the experimental tasks were similar to the practice ones. The low stress condition was identical

to the practice trials with the exceptions that (1) each trial was twice as long (10 min vs. 5 min), and (2) the specific numbers required for a correct response were changed.

In the high stress condition, the 10-min trials differed from the practice trials in two ways. First, unknown to the participants, no numeric code would change the screen from red to white; the task was impossible to solve. Each participant in the high stress condition was yoked to a participant in the low stress condition such that the pattern of screen changes in the high stress condition matched that of one participant in the low stress condition with a similar depression history. Second, when the screen was red, an aversive tone at 3000 Hz and 90 dB was delivered over the earphones. This noise began 2.5 s after the screen turned red and remained on until the screen turned white. Thus, high stress was created by the absence of control over the screen and by prolonged exposure to an aversive noise.

1.2. Measures

1.2.1. Structured Clinical Interview for Diagnosis—DSM-IV (SCID; First et al., 1995)

The SCID, a semi-structured interview, allows for current and lifetime diagnoses of Axis I disorders according to DSM-IV criteria (APA, 1994). All SCID interviews were conducted by one of the authors (M.A.I.) who was an advanced clinical psychology graduate student at the time of the study and who had received extensive training and supervision in the administration of the SCID. Inter-rater agreement (overall weighted kappas) for current and lifetime MDD were reported by Williams et al. (1992) as 0.64 and 0.69, respectively.

1.2.2. Demographics questionnaire

Self-report measures were used to collect information on age, sex, marital status, Social Economic Standing (SES), occupation, income, education, and race.

1.2.3. Beck Depression Inventory II (BDI-II; Beck et al., 1996)

The BDI-II is a 21-item self-report questionnaire designed to measure the presence and severity of symptoms of depression consistent with the DSM-IV (APA, 1994). Beck et al. (1996) report high internal consistency (mean coefficient alpha=0.93 for college students) and test–retest reliability (0.93 for a 1-week interval). In the current sample, coefficient alpha was 0.77.

1.2.4. Self-report stress

Experienced stress was assessed via a single-item administered after each trial of the computer task. The scale asked participant to rate their level of stress on a 10-point scale ranging from “no stress” (coded 1) to “very stressed” (coded 10). This measure was used as a manipulation check to test the impact of the stress manipulation on perceived stress.

1.2.5. Profile of Mood States (POMS; McNair et al., 1971)

This is a 65-item, 5-point adjective rating scale that measured fluctuations in mood over short times periods. Two subscales of the POMS were used: the depression subscale and the tension subscale. Pre-test coefficient alphas were 0.87 and 0.83 for the depression and tension subscales, respectively.

1.2.6. Self-report of perceived control

Participants were asked to estimate the amount of control that they had over the task. The scale asked, “How much control did you have over the computer?” Responses ranged from “no control” (coded 1) to “full control” (coded 10).

1.2.7. Behavioral indicators

The number of responses made during each repetition of the task was used to investigate behavioral effects of high and low stress conditions. Analyses of this information used the number of responses given during full 15-s trials of the red screen. This was done to hold constant the length of time allowed to enter answers for all participants.

1.3. Data analysis

For the primary data analyses, separate 2 (no past MDD, past MDD)×2 (low stress, high stress)×4 (trials 1–4) repeated measures analyses of covariance (ANCOVAs) were conducted with pre-test scores of each measure included as covariates. The dependent variables were: rating of stress, POMS depression and tension, and number of guesses made during each full

trial of the task. A similar repeated measures ANOVA was conducted for control over the task.

2. Results

Initial analyses were conducted to determine whether there were baseline differences between the groups based on assignment to the stress condition. Table 1 presents baseline data for the overall sample and broken down by experimental condition and prior history of depression. No significant differences were found between the low and high stress conditions. Participants with a history of depression reported more baseline depressive symptoms on the BDI than did non-depressed participants [$F(1, 60)=5.4$, $p<0.05$]. After completing all analyses described below a set of identical analyses were run with baseline BDI as a covariate in order to control for baseline depressive symptoms. None of the results were significantly changed by the inclusion of BDI as a covariate.

2.1. Self-report stress

The means of the self-reported stress by condition are presented in Fig. 1. There was a strong main effect of stress condition on self-report ratings of stress controlling for baseline stress [$F(1, 57)=17.55$, $p<0.01$] those in the high-stress condition reported significantly more stress following the experimental manipulation than did those in the low-stress condition. No other main effects or interaction effects were found. These findings indicate that the stress manipulation was successful.

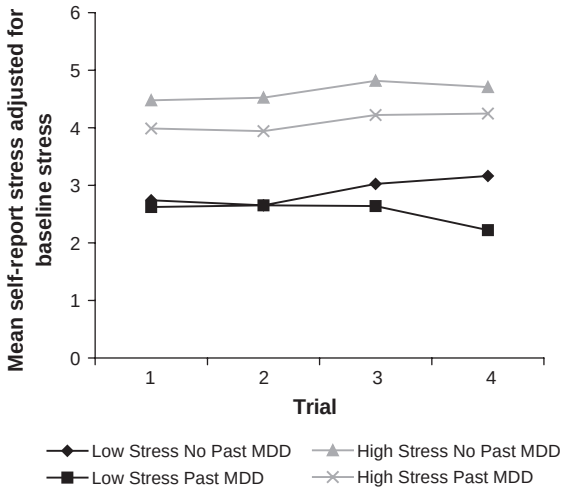

Fig. 1. Mean self-reported ratings of stress across all four experimental trials adjusting for baseline ratings of stress.

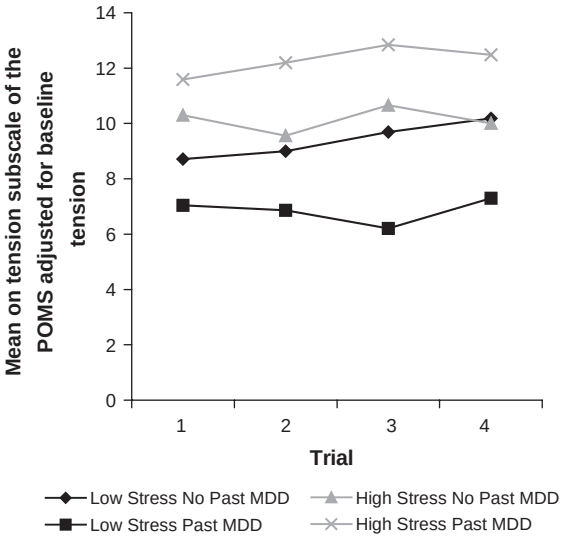

Fig. 2. Mean self-reported ratings of tension as measured by the POMS across all four experimental trials adjusting for baseline ratings of tension.

2.2. The POMS

On the tension subscale of the POMS, there was a main effect of stress condition when controlling for baseline tension [$F(1, 57)=9.13$, $p<0.01$] such that individuals in the high stress condition reported more tension than did those in the low stress condition (see Fig. 2). There was no main effect of history of MDD on the tension subscale of the POMS. A significant interaction was found between stress level and depression [$F(1, 57)=5.37$, $p<0.05$] on the tensions subscale of the POMS. Subsequent comparisons indicated that those with a history of MDD in the high stress condition reported significantly more tension than other participants [$t(1, 57)=8.15$, $p<0.01$] and those with a history of MDD in the low stress condition reported significantly less tension than other participants [$t(1, 57)=9.29$, $p<0.01$].

For all analyses of the depression scale of the POMS, no significant main effects or interaction effects were found.

2.3. Perceived control

Participant reports of control are presented in Fig. 3. Participants in the low stress condition reported greater control over the task than those in the high stress condition [$F(1, 57)=6.81$, $p<0.01$]. Ratings of control for the entire sample decreased significantly over time [$F(3, 174)=3.11$, $p<0.05$]. A significant interaction between level of stress and time [$F(3, 174)=2.84$, $p<0.05$] indicated that feelings of control in the high stress condition decreased over time while those in the low stress condition stayed relatively stable.

2.4. Behavioral measures of performance on the task

During the task, the computer recorded the number of attempts per trial made by each participant. Data for 60 participants were complete and used in the following analyses. No significant main effects for history of MDD or level of stress were found. As seen in Fig. 4, a significant interaction existed between stress level and history of MDD [$F(1, 58)=5.16$, $p<0.05$]. Subsequent comparisons indicate that this interaction was due to a high level of responding in the group without a history of depression in the high stress condition [$t(1, 57)=9.13$, $p<0.01$] compared to all other participants. Thus, those participants in the high stress condition without a history of MDD responded to uncontrollable stress by responding at a significantly higher rate on the task while those individuals with a history of MDD responded to uncontrollable stress by maintaining a relatively low level of responding.

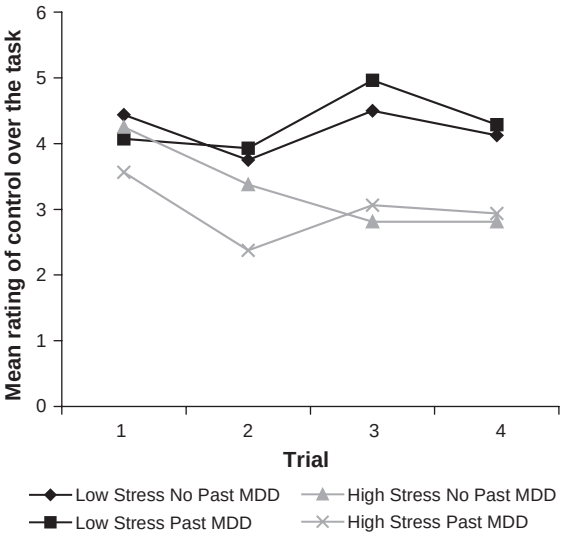

Fig. 3. Self-report of perceived control across all four experimental trials.

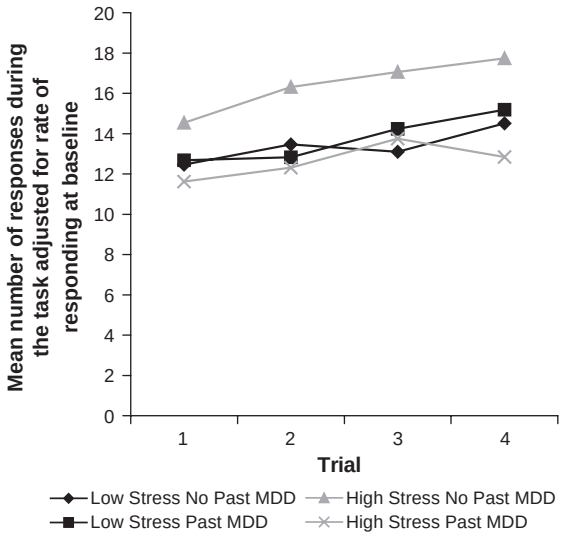

Fig. 4. Mean number of guesses recorded during trials of the computer task across all four experimental trials adjusting for the number of guesses made during the baseline trial.

3. Discussion

The primary finding of the present study was that individuals with a history of MDD responded differently to uncontrollable stress than did those without a history of MDD. This was apparent in both self-report measures of tension and behavioral measures of task performance for participants with a history of MDD randomly assigned to the high stress condition.

Our finding that individuals with a history of MDD had an increased sensitivity to stress extends the existing literature by demonstrating that the vulnerability to stress in those with past MDD is not only related to major life stressors (e.g., low achievement, loss of a significant relationships, etc.) but also evident when exposed to more minor stressors.

The opportunity to characterize the behavioral sequelae associated with an increased sensitivity to a

laboratory stressor was a novel contribution of the present study. The findings suggest that individuals with a history of MDD responded to stress by decreasing their effort on a challenging task whereas those without past depression displayed a clear increase in the number of responses given. The degree to which this response is adaptive or maladaptive is unknown at this time. However, the data fit a learned helplessness model of depression (Abramson et al., 1978) in which individuals with depression tend to "give-up" in the face of a challenge instead of trying harder to overcome it. Over time, it is possible that this pattern of decreased effort in the face of challenges may lead to an increase in the number of negative experiences that one might face. Although the factors associated with a recurrence of MDD are just beginning to be understood (e.g., Hart et al., 2001), this study provides evidence that differential behavioral responses to an acute stressor may be an important factor in understanding how different cognitive styles often observed in those with a history of MDD (e.g., Alloy et al., 1999) may lead to a change in behavior and ultimately a recurrence of the disorder.

In general, past research on the learned helplessness or hopeless theory of depression has concentrated on the relationship between stress, attributional style and depressive symptoms or a depressive episode (e.g., Lewinsohn et al., 2001; Peterson and Vaidya, 2001). In the present study, effects of the stress manipulation were seen in ratings of tension and behavioral measures of performance but were not detected in measures of depressed affect. Thus, the present findings indicate behavioral measures may be more sensitive than measures of depressed affect and may represent an important focus for future research on diathesis-stress models of depression. For clinicians, attending to maladaptive behavioral responses to even minor stressors may be particularly important when treating those with a history of MDD.

An additional contribution of this study was the development of a laboratory task that produced reliable differences in self-report measures of stress when stress level was manipulated. Although the use of stress manipulation has yielded numerous important findings in the animal literature (i.e., Overmier and Seligman, 1967), the human literature uses primarily psychosocial stressors (for a review, see Linden, 1998). A possible confounding factor when using psychosocial stressors is that MDD has been associated with a high degree of interpersonal sensitivity (e.g., Boyce et al., 1993). This makes disentangling the impact of the interpersonal aspects of a psychosocial stressor from the "pure" stress-related impacts particularly difficult. Consequently, a reliable, non-social laboratory stressor should be a useful tool for comparing human and animal research on stress.

The generalizability of our stress manipulation to real world stressors is not known. Additionally, the fact that participants still reported some level of control over the task raises concerns over whether or not a failure to sense control played a direct causal role in the affective and behavioral differences seen between groups. Future research using this stress manipulation would benefit from improved measures of self-report stress, the cognitive styles of participants, their motivation and perception of the task, and physiological measures of stress responsivity. An additional limitation of the study was that the present sample was quite homogeneous in age and ethnicity, and results from this sample may not generalize well to other individuals. Concerns about generalizability also apply given the fact that the study was conducted as part of a larger research project that included the administration of alcohol. It is not known how this may have influenced the results presented here. More work needs to be done to extend this work to more diverse samples with both current and past MDD.

Despite these limitations, the present study provides a novel first attempt to describe the responses of previously depressed individuals to a stress manipulation. More research is needed to understand how the increase sensitivity to stress that has been described in the clinical literature (e.g., Kendler et al., 1999; Lewinsohn et al., 1999) influences the daily experience and behavior of individuals with a history of MDD.

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